consisting of SEQ NOS: 280, 317, 337, 384, 465, and 488 and complements thereof.

32. (Amended) A method for measuring the carcinogenicity of a composition comprising:

(A) exposing a cell, tissue sample, or test mammal to said composition; and

(B) determining the presence or absence of mRNA which substantially hybridizes to an at least one nucleic acid sequence selected from the group consisting of SEQ NOS: 280, 317, 337, 384, 465, and 488 and complements thereof.

34. The method of claim 33, wherein said cell, tissue sample, or test mammal comprises a rat hepatocyte.

35. The method of claim 32, wherein said cell, tissue sample, or test mammal comprises a rat hepatocyte.

REMARKS

Rejection under 35 U.S.C. § 112, first paragraph

Reconsideration and withdrawal of rejection of claims 25-28 and 31-33 under 35 U.S.C. § 112 is respectfully requested.

On page two of the Office Action, the Examiner rejected claims 25-28 and 31-33 under 35 U.S.C. § 112, first paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, and claims 25-27 and 31-33 for failing to reasonably provide enablement:

I. The office has asserted that in Claim 25, the term "conditions permitting nucleic acid hybridization" is unclear. "The phrase 'conditions permitting nucleic acid hybridization' in line 3 of claim 25 is unclear and needs to be clarified."

Applicants respectfully disagree with this assertion and requests withdrawal

of this objection for the following reasons:

The term "conditions permitting nucleic acid hybridization" is definite. The conditions permitting nucleic acid hybridization are well known in the art (See, for example, Sambrook *et al.*, discussed on page 12, lines 16-20 and Ausubel *et al.*, discussed on page 13, lines 1-7 of the specification). Further, appropriate conditions for permitting DNA hybridization are discussed on page 13, lines 1-12.

The art and the specification clearly identify the conditions permitting nucleic acid hybridization, and therefore the phrase apprises those skilled in the art of the scope of the invention.

Therefore, Claim 25 is submitted as patentable.

II. The office has asserted that In Claims 31 and 32, the term "substantially hybridizes" is unclear. "The phrase 'substantially hybridizes' in lines 4 and 5 of claims 31 and 32 is unclear and needs to be clarified."

Applicant respectfully disagrees with this assertion and requests withdrawal of this objection for the following reasons:

The term "substantially hybridizes" is defined on line 5, page 9, to mean "that two nucleic acid molecules can form an anti-parallel, double-stranded nucleic acid structure under conditions (e.g. salt and temperature) that permit hybridization of sequences that exhibit 90% sequence identity or greater with each other and exhibit this identity for at least a contiguous 50 nucleotides of the nucleic acid molecules."

Therefore, Claim 31 and 32 are submitted as patentable.

III. The office has asserted that claims 25-27 and 31-33 do not reasonably provide enablement for a method for determining a level or pattern of a carcinogenesis biomarker in any cell. "Claims 25-27 and 31-33 are rejected under 35 U.S. C. 112, first paragraph, because the specification, while being enabling for observing the differences in the expression of various transcripts in liver cells obtained from rats following their exposure to Phenobarbital, does not reasonably provide enablement for a

method for determining a level or pattern of a carcinogenesis biomarker in any cell."

Applicant respectfully disagrees with this assertion and requests withdrawal of this objection for the following reasons:

The Examiner states that the examples provided in the instant specification are not generally applicable to the neoplastic transformation of all cell types following their exposure to any and/or all carcinogenic agents. The Examiner has not made the prima face case for non-enablement. There is no showing that the applicants' invention does not work.

The Examiner further states that there is a high level of unpredictability that exists in comparing mRNA abundances with protein abundances for a given cell type. The claims under consideration are not directed to identifying protein, nor to correlating protein level with carcinogenicity. Rather, they are directed to identifying the amount mRNA in a cell to determine a level or pattern of a carcinogenesis biomarker.

Therefore, Claims 25-27 and 31-33 are submitted as patentable.

Rejections under 35 U.S.C. § 102

Reconsideration and withdrawal of rejection of claims 25-28 under 35 U.S.C. § 102 is respectfully requested.

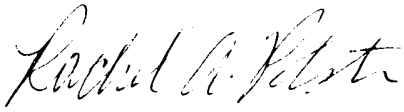
On page seven of the Office Action, the Examiner rejected claims 25-28 under 35 U.S.C. § 102 (e) as being anticipated by Hillman *et al.*, under 35 U.S.C. § 102 (b) as being anticipated by Upton *et al.*, under 35 U.S.C. § 102 (b) as being anticipated by Lee *et al.*, and 35 U.S.C. § 102 (b) as being anticipated by Skoda *et al.*

The applicants have amended claims 25-28, which are submitted as patentable.

Claims 25-28 and 31-33 are pending, and submitted as patentable. New claims 34 and 35 have been added. Claim 34 depends from claim 33, which has been submitted as patentable, and claim 35 depends from claim 32, which is also submitted as patentable. Therefore claims 34 and 35 are submitted as patentable.

In view of the foregoing amendment and remarks, all claims now active in the present application are in condition for allowance. Therefore, passage of the application and claims to issue is respectfully requested.

Respectfully submitted,



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PATENT Case SO-3170-US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:	
Bunch, R. T. et al.	GROUP ART UNIT: 1635
SERIAL NUMBER: 09/490,609	EXAMINER: J. Zarra
FILED: January 25, 2000	DATE: February 13, 2002

TITLE: BIOMARKERS AND ASSAYS FOR CARCINOGENESIS

APPENDIX TO AMENDMENT
Version of Claims With Markings To Show Changes Made

25. (Amended) A method for determining a level or pattern of a carcinogenesis biomarker in a cell comprising:

(A) incubating, under conditions permitting nucleic acid hybridization, a marker nucleic acid molecule, said marker nucleic acid molecule having a nucleic acid sequence selected from the group consisting of [SEQ NO:1 through SEQ NO: 580] SEQ NOS: 280 and 488 or complements thereof, with a complementary nucleic acid molecule obtained from said cell, wherein nucleic acid hybridization between said marker nucleic acid molecule, and said complementary nucleic acid molecule obtained from said cell permits the detection of said carcinogenesis biomarker;

(B) permitting hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said cell; and

(C) detecting the level or pattern of said complementary nucleic acid, wherein the detection of said complementary nucleic acid is predictive of the level or pattern of said carcinogenesis biomarker.

31. (Amended) A method for measuring the carcinogenicity of a composition comprising:

(A) culturing a cell line;

(B) exposing said cell line to said composition; and

(C) determining the presence or absence of mRNA which substantially hybridizes to an at least one nucleic acid sequence selected from the group consisting of [SEQ NO: 1 through SEQ NO: 580] SEQ NOS: 280, 317, 337, 384, 465, and 488 and complements thereof.

32. A method for measuring the carcinogenicity of a composition comprising:

(A) exposing a cell, tissue sample, or test mammal to said composition; and

(B) determining the presence or absence of mRNA which substantially hybridizes to an at least one nucleic acid sequence selected from the group consisting of [SEQ NO:1 through SEQ NO:580] SEQ NOS: 280, 317, 337, 384, 465, and 488 and complements thereof.

33. The method of claim 32, wherein said mammal is a rat.

Please insert the following claims 33 and 35:

34. The method of claim 33, wherein said cell, tissue sample, or test mammal comprises a rat hepatocyte.

35. The method of claim 32, wherein said cell, tissue sample, or test mammal comprises a rat hepatocyte.